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**IN THE UNITED STATES DISTRICT COURT
DISTRICT OF UTAH, CENTRAL DIVISION**

UNIVERSITY OF UTAH RESEARCH
FOUNDATION et al.

Plaintiffs,

vs.

AMBRY GENETICS CORPORATION,
Defendant.

UNIVERSITY OF UTAH RESEARCH
FOUNDATION et al.

Plaintiffs,

vs.

GENE BY GENE LTD.,
Defendant.

**DECLARATION OF JONATHAN F.
TAIT, M.D., PH.D. IN SUPPORT OF
DEFENDANTS AMBRY GENETIC
CORPORATION'S AND GENE BY
GENE LTD'S OPPOSITION TO
PLAINTIFFS' MOTION FOR
PRELIMINARY INJUNCTION**

CASE No. 2:13-cv-00640-RJS
CASE No. 2:13-cv-00643-RJS

Honorable Robert J. Shelby

I, Jonathan F. Tait, M.D., Ph.D., state and declare:

1. I am Professor of Laboratory Medicine; Head, Genetics Division, Laboratory Medicine; Vice Chair, Academic Affairs, Department of Laboratory Medicine; Adjunct Professor of Pathology; Adjunct Professor of Medicine/Medical Genetics – all at the University of Washington.

2. I have been retained by the defendants and their counsel as a consulting expert for this case. I have received no compensation for my services.

3. I received my bachelor's degree from Harvard University, my M.D. and Ph.D. degrees from Washington University (St. Louis), my pathology residency and fellowship postgraduate training from the University of Washington (Seattle).

4. I have been on the faculty of the University of Washington continuously since 1987.

5. I am board certified in Clinical Pathology, and I am a member of the medical staffs at the University of Washington Medical Center and the Seattle Cancer Care Alliance.

6. I am a member of the Washington State Medical Association, the Association for Molecular Pathology, and the Academy of Clinical Laboratory Physicians and Scientists.

7. I participate in professional association committees that set standards for clinical laboratories, most recently in the Personalized Healthcare Committee of the College of American Pathologists.

8. I have published over 110 peer-reviewed scientific articles.

9. A copy of my curriculum vitae is attached hereto as Exhibit A.
10. In my current position, I direct the work of a group of about sixteen faculty and staff who provide state-of-the art clinical genetic testing services in the Genetics and Solid Tumors Laboratory at the University of Washington Medical Center. I founded this laboratory in 1986, and I have directed it continuously for the last 27 years. This laboratory provides a broad menu of genetic tests to physicians and other health care providers. This laboratory is also an integral part of clinical education and training in molecular diagnostics for medical students, medical residents and clinical fellows at the University of Washington. This laboratory is also a key resource for clinical research related to genetic testing.

MATERIALS REVIEWED

11. I have reviewed the *Motion for Preliminary Injunctive Relief and Memorandum In Support* filed by Myriad Genetics, Inc. and other plaintiffs (collectively, “Myriad”) (Dkt. No. 5) in the case against Ambry Genetics Corp. (“Ambry”) in the District of Utah (Case No. 2:13-cv-00640-RJS). I understand that Myriad’s Motion for Preliminary Injunctive Relief relates to claims of patent infringement asserted by Myriad against Ambry in the case.

12. I have reviewed the patent claims asserted in support of Myriad’s Motion for Preliminary Injunctive Relief and the Declaration of Benjamin B. Roa cited in support of same, which includes Myriad’s general contentions as to why Myriad believes the claims described are infringed and why Myriad believes those claims are valid.

13. I have also reviewed the U.S. Supreme Court's decision in the case named *Association for Molecular Pathology v. Myriad Genetics*, 529 U.S. __ (2013) and lower court opinions. I understand that the Supreme Court ruled that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but that cDNA is patent eligible because it is not naturally occurring. Stated another way, the Court determined that "genes and the information they encode are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material." *Id.*

14. I understand that the Supreme Court decision involved claims directed to isolated DNA and that the Court made the following clarification:

[T]here are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent. But the processes used by Myriad to isolate DNA were well understood by geneticists at the time of Myriad's patents 'were well understood, widely used, and fairly uniform insofar as any scientist engaged in the search for a gene would likely have utilized a similar approach...and are not at issue in this case.'

Similarly, this case does not involve patents on new applications of knowledge about the BRCA1 and BRCA2 genes."

15. I have also reviewed the U.S. Supreme Court's decision in the case named *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012). I understand that in the *Prometheus* case, the Court addressed whether the inclusion of additional steps of the claimed processes at issue had transformed an unpatentable natural law into patent-eligible applications of those laws. I understand that the Supreme Court held that "appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Id.* at 1300. I understand that such is the case when the "steps consist of well-understood, routine,

conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately.” *Id.* at 1298.

The Claims Asserted in Myriad’s Motion for Preliminary Injunction

16. I understand that Myriad’s Motion for Preliminary Injunctive Relief is based on Myriad’s assertion, in part, that Myriad is likely to prove that Ambry unlawfully infringes the following patent claims, which Myriad asserts are valid:

- Claims 16 and 17 of U.S. Patent No. 5,747,282 (earliest filing date Aug. 12, 1994);
- Claims 7 and 8 of U.S. Patent No. 5,753,441 (earliest filing date Aug. 12, 1994);
- Claims 29 and 30 of U.S. Patent No. 5,837,492 (earliest filing date Dec. 12, 1995);
- Claim 4 of U.S. Patent No. 6,033,857 (earliest filing date of Dec. 12, 1995);
- Claim 5 of U.S. Patent No. 6,951,721 (earliest filing date of Feb. 12, 1996); and
- Claims 2 and 4 of U.S. Patent No. 5,654,155 (filed Feb. 12, 1996).¹

17. Claims 7 and 8 of the ’441 patent (“method(s) for screening germline of a human subject for alteration of a BRCA1 gene...”), claim 4 of the ’857 patent (“A method for diagnosing a predisposition for breast cancer in a human subject...”), claim 5 of the ’721 patent (“A method for determining an omi haplotype of a human BRCA1 gene ...”); and claims 2 (“A method of identifying individuals having a BRCA1 gene with a BRCA1 coding sequence not

¹ I offer no opinion in this declaration as to whether any of the claims asserted by Myriad in the lawsuit against Ambry are entitled to priority dates consistent with the earliest filing dates associated with the applications that led to the issuance of the patents discussed in this declaration.

associated with breast or ovarian cancer...") and claim 4 ("A method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA1 coding sequence...") of the '155 patent are all method claims.

18. Each of claims 16 and 17 of the '282 patent and claims 29 and 30 of the '492 patent claim "a pair of single-stranded DNA primers for determination of a nucleotide sequence...using a polymerase chain reaction..."

The Asserted Method Claims

19. Each of the method claims asserted in Myriad's Motion for Preliminary Injunctive Relief share a common feature. Namely, each of the claims specifies that the respective methods are performed by comparing the sequence of the native DNA obtained from a patient sample, to a reference DNA sequence that may also be found in the BRCA1 or BRCA2 genes in human cells (either "wild type" or altered DNA). In all cases, the gene sequences recited in the asserted claims are directed to human DNA sequences.²

20. Similarly, the subject matter of each asserted method claim depends solely on the specific sequence including or surrounding the relevant BRCA gene obtained from the patient sample. That is, the result of the respective methods is dictated by the identity of the patient-specific gene(s) and the genetic information they encode.

² I note that some of the claims raise the possibility of using cDNA made from an mRNA as a sample, e.g., claim 8 of the '441 patent. However, the claims address the samples in the alternative, i.e., either genomic or cDNA may be used.

21. In addition to each of the “comparison” steps specified as part of the asserted methods claims, each of the claims generally recites steps or limitations related to preparing and observing the patient sample as part of a determination of the sequence of the DNA obtained from a patient sample. These related steps include “hybridization,” “amplification,” and/or “sequencing” of the patient sample. I discuss each of the three additional limitations further below.

22. **Hybridization** – Hybridization (or annealing) is a well-known, natural phenomenon that results from “Watson-Crick base pairing” between two complementary strands of nucleic acids. Hybridization, a form of binding between molecules, occurs as a result of the inherent chemical properties of nucleic acid molecules, and gives double-stranded DNA its characteristic helical structure, which was first identified by Drs. James Watson and Francis Crick and x-ray crystallographer Rosalind Franklin in the early 1950’s.³ By the time that the scientists had discovered the structure of DNA, its hereditary properties had already been discovered.⁴

23. **Probes and Primers** – Single-stranded segments of DNA may be used by researchers as probes for determining the presence or absence of specific DNA sequences in a sample. Single-stranded segments of DNA are also routinely used as primers for “amplification” (copying) of DNA template in well-known laboratory procedures such as the “Polymerase Chain

³ Watson, J.D and Crick, F.H.C., Molecular Structure of Nucleic Acid: A Structure for Deoxyribose Nucleic Acid. *Nature* 171:737-38 (1953); Wilkins M.H.F., A.R. Stokes A.R. & Wilson, H.R., Molecular Structure of Deoxypentose Nucleic Acids. *Nature* 171: 738-40 (1953); Franklin R. and Gosling R.G., Molecular Configuration in Sodium Thymonucleate. *Nature* 171: 740-41 (1953); Watson J.D. and Crick F.H.C., Genetical Implications of the structure of Deoxyribonucleic Acid. *Nature* 171: 964-67 (1953).

⁴ Avery, O.T., MacLeod, C.M. & McCarty, M., Studies on the chemical nature of the substance inducing transformation of Pneumococcal types. *J. Exp. Med.* 79:137-59 (1944).

Reaction (PCR)” method and “Sanger Sequencing” method (both discussed further below). The use of a segment of DNA as a probe or a primer relies on the natural phenomenon of hybridization.

24. The composition of a probe or a primer is largely dictated by the sequence that a researcher may want to observe, either directly or indirectly, through a variety of available laboratory techniques. The composition of the probe or primer is determined based on the specificity with which the researcher would like to identify certain portions of DNA through the laboratory procedures, and the fidelity with which the researcher would like in preparing copies of DNA through amplification. For purposes of genetic testing, the investigator typically desires highly stringent (or specific) hybridization for qualitative analysis and high fidelity amplification.

25. Generally, longer DNA oligonucleotide probes or primers that have exact complementarity to their DNA target will result in relatively more specific hybridization to a target molecule than would shorter oligonucleotide probes or primers that may have one or more nucleotide base mismatches with the DNA target. The specificity of the oligonucleotide to its complementary DNA target is dictated by the natural laws of thermodynamics. Frequently, the specificity of a complementary primer is described in terms of the primer’s “melting

temperature,”⁵ when compared with its target sequence, which may be approximated through a simple mathematical formula.⁶

26. Generally, a probe is used to detect the presence or absence of a particular DNA sequence in a sample of DNA. The creation and use of synthetic DNA probes in genetic testing experiments was well-known and commonplace by the time that Myriad applied for the earliest patent at issue in its Motion for Preliminary Injunction.⁷

27. **Amplification** – DNA oligonucleotide primers are called primers because they “prime” an enzymatic reaction catalyzed by a naturally-occurring enzyme called DNA polymerase. DNA polymerase is ubiquitously found in cells. The function of DNA polymerase, both in a cell (in vivo) and in a test tube (in vitro), is to make a complementary, duplicate copy of a DNA transcript. DNA “sense” strands are read from their 5’ ends to their 3’ ends. The complementary “antisense” strand is also read from the 5’ to 3’ directions. The DNA polymerase creates the DNA polymer comprised of individual nucleotides by recognizing that a partially double-stranded molecule of DNA is not completely double stranded. The DNA polymerase acts to complete the complementary strand of the transcript by adding complementary nucleotides from the 5’ to the 3’ end of a growing, complementary strand of

⁵ See Marmur, J. and Doty, P. Determination of the base composition of deoxyribonucleic acid from its thermal denaturation temperature. *J. Mol. Biol.* 5:109-18 (1962).

⁶ See Wallace, R.B. et al., Hybridization of synthetic oligodeoxyribonucleotides to phi chi 174 DNA: the effect of single base pair mismatch. *Nucleic Acids Research* 6(11): 3543-57 (1979). The formula is $T_m = 4(G + C) + 2(A + T) \text{ } ^\circ\text{C} + 8\text{ } ^\circ\text{C}$ for primers used in an aqueous solution that are approximately 15-40 nucleotides long.

⁷ See, e.g., Itajura, K. et al. Synthesis and Use of Synthetic Oligonucleotides. *Annual Review of Biochemistry*. 53: 323-56 (1984); Wallace RB, Studencki AB, Murasugi A.J. Application of synthetic oligonucleotides to the diagnosis of human genetic diseases. *Biochimie*. 67:755-62 (1985). Sambrook, E.F. Fritsch, T. Maniatis, *Molecular Cloning : A Laboratory Manual* 2nd ed. (1987).

DNA. The function of the DNA polymerase is for replication of genomic DNA and may also serve as a repair function for DNA that becomes damaged.

28. Scientists use DNA polymerase along with other commercially available reagents in the laboratory to amplify DNA targets of interest for a variety of reasons, *e.g.*, for quantitative analysis, or qualitative analysis, or for preparative reasons, or a combination of all three. Amplification, generally, and the laboratory materials, reagents, and protocols to accomplish same were well known and widely available in the art by the time the first patent application corresponding to the asserted patents had been filed.

29. **Polymerase Chain Reaction (PCR).** PCR is a laboratory method that relies on successive cycles of hybridization of DNA primers to a DNA template and concomitant amplification via DNA polymerase. The cycles are mediated through changes in temperature that allow for melting, annealing, and amplification. PCR was invented in the 1980's by Dr. Kary Mullis at Cetus Corporation.⁸ In 1989, the prestigious journal *Science* identified PCR and its use of a DNA polymerase from a thermophilic bacterium, *Thermus aquaticus* (*Taq* DNA polymerase), as the "Molecule of the Year."⁹ Dr. Mullis won the Nobel Prize in Chemistry for his invention in 1993.¹⁰

⁸ U.S. Patent No. 4,683,202 (Mullis, K.) titled PROCESS FOR AMPLIFYING NUCLEIC ACID SEQUENCES was filed on Oct. 25 1985 and issued on July 28, 1987. *See also*, Saiki R.K. and Mullis K.B. *et al.*, Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. *Science*. 230(4732):1350-4 (1985); Mullis K.B. and Faloona F.A., Specific synthesis of DNA in vitro via a polymerase-catalyzed chain reaction. *Methods Enzymol.* 155:335-50 (1987).

⁹ Koshland, DE. The Molecule of the Year. *Science*. 246:1541 (1989); Saiki R.K. and Mullis K.B. *et al.*, Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. *Science*. 239:487-491 (1988)(describing the use of a thermophilic DNA polymerase, which resulted in the ability to automate the PCR process).

¹⁰ "Kary B. Mullis – Facts." Nobelprize.org. Nobel Media AB 2013. Web. 28 Jul 2013. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1993/mullis-facts.html>

30. PCR was a transformative invention that changed the course of modern biological and biochemical investigation, including R&D, diagnostics, forensics, and pathology. In 1998, the N.Y. Times published a biographical article on Dr. Mullis stating that Dr. Mullis' "invention is highly original and significant, virtually dividing biology into the two epochs of before P.C.R. and after P.C.R."¹¹

31. Based on my experience, PCR was a well-understood, routine, conventional activity already engaged in by the scientific community by the time the first patent application corresponding to the asserted patents had been filed and prior to the identification of the BRCA1 or BRCA2 gene sequences. In 1990 and 1991, I personally published three research articles in peer-reviewed journals describing the use of PCR in diagnostic methods in the field of molecular genetics.¹² In those articles, I described how PCR was used on patient samples to detect genetic abnormalities that could or would cause a particular disease in the patient, including cystic fibrosis and sickle cell disease. The articles that I published were hardly unique in the sense that they utilized PCR for molecular genetic testing; the PCR technique was widely used at that time.

32. **Information Encoded by DNA.** DNA encodes heritable biological information organized into functional segments that are commonly referred to as "genes." The heritable information that is part of an organism's genome (that is, "the whole of the genetic information

¹¹ Wade, Nicholas (September 15, 1998), "Scientist at Work/Kary Mullis; After the 'Eureka', a Nobelist Drops Out," The New York Times.

¹² Skogerboe KJ, West SF, Murillo MD, Tait JF. PCR dot blots: large signal differences between sense and anti-sense probes. *Biotechniques*. 9:154 (1990); Skogerboe KJ, West SF, Murillo MD, Tait JF. Development and evaluation of a simplified dot-blot method for detecting the delta F508 mutation in cystic fibrosis. *Clin Chem*. 36:1984-6 (1990); Skogerboe KJ, West SF, Murillo MD, Glass MW, Shaunak S, Tait JF. Genetic screening of newborns for sickle cell disease: correlation of DNA analysis with hemoglobin electrophoresis. *Clin. Chem.* 37:454-8 (1991); *see also* Saiki, R. K., Bugawan, T. L., Horn, G. T., Mullis, K. B., & Erlich, H. A.. Analysis of enzymatically amplified β -globin and HLA-D α DNA with allele-specific oligonucleotide probes. *Nature*, 324(6093), 163-166 (1986)(describing hybridization and amplification technique)

of an organism") is conveyed through the sequence of the nucleotides that comprise the individual genes. Every cell in the human body contains a complete copy of the human's genome. The unique, informational characteristic of DNA sets it apart from other biological molecules, which imparts obvious significance to the otherwise inert material.

33. The encoded information of DNA is manifested by "expression" of the gene within the cell, typically in the form of proteins, through a well-known process described by Dr. Francis Crick as the "Central Dogma," which relies on the use of messenger RNA (mRNA) as an intermediary.

34. Proteins perform discrete cellular functions such as catalyzing (speed up) chemical reactions, or providing structural functionality. A protein's functionality is dictated by its amino acid composition, which is, in turn, dictated by nucleotide sequence that encodes the protein. The complete "genetic code" has been known since 1966.¹³ Disease conditions in humans frequently are due to mutations or alterations in an individual's copy of a single gene that gives rise to a protein that is different from the normal (or "wild type") protein that is expressed in persons without the disease. The genetic mutation that is responsible for such protein alteration may be determined, and may be observed relatively easily through analysis of a patient's DNA sequence from a patient sample.

¹³ See Jones, O. W., & Nirenberg, M. W., Degeneracy in the amino acid code. *Biochimica et Biophysica Acta.*, 119(2), 400-06 (1966) (reporting completion of the genetic code, and describing its "degeneracy"). Marshall Nirenberg was awarded the Nobel Prize in Medicine in 1968 for his work in deciphering the genetic code.

35. **Sequencing.** “Sequencing” refers to the act of determining the sequence of one or more segments of DNA using one of a variety of laboratory techniques. While other techniques existed at the time,¹⁴ a technique called “Sanger Sequencing” (also referred to as “dideoxy sequencing”) had become the most prevalent sequencing technique in modern labs by the time that Myriad had applied for the first of the patents asserted in its Motion for Preliminary Injunction.¹⁵ Of the method claims asserted against Ambry in the Motion for Preliminary Injunction that specifically require performance of DNA sequencing by Ambry to infringe,¹⁶ only claims 2 and 4 of the ‘155 patent specify a particular variety of sequencing—“dideoxy sequencing.” The composition claims do not require sequencing to be performed at all. Instead, they recite only that the “DNA primers [are] for determination of a nucleotide sequence by a polymerase chain reaction.” ’282 patent, claims 16 and 17; *see also* claims 29 and 30 (using similar language).

36. Improvements in the Sanger method by 1987 led to automation of the sequencing process.¹⁷ These Sanger Sequencing methods were used widely well prior to the time the first patent applications corresponding to the asserted patents had been filed and prior to the identification of the *BRCA1* or *BRCA2* gene sequences.

¹⁴ See, e.g., Maxam, A. M., & Gilbert, W. A new method for sequencing DNA. *Proceedings of the National Academy of Sciences*, 74(2), 560-564 (1977).

¹⁵ Sanger, F., Nicklen, S., & Coulson, A. R. DNA sequencing with chain-terminating inhibitors. *Proceedings of the National Academy of Sciences*, 74(12), 5463-5467 (1977).

¹⁶ Such claims include: claim 8 of the ‘441 patent, claim 4 of the ’857 patent (as it is asserted by Myriad); claim 5 of the ’721 patent, claims 2 and 4 of the ‘155 patent.

¹⁷ Prober, James M., et al. A system for rapid DNA sequencing with fluorescent chain-terminating dideoxynucleotides. *Science*. 238: 336-41(1987); *See also*, Zimmermann, J., Voss, H., Schwager, C., Stegemann, J., & Ansorge, W.. Automated Sanger dideoxy sequencing reaction protocol. *FEBS letters*.233(2), 432-436 (1988); Kristensen, T., Voss, H., Schwager, C., Stegemann, J., Sproat, B., & Ansorge, W.. T7 DNA polymerase in automated dideoxy sequencing. *Nucleic acids research*, 16(8), 3487-3496 (1988).

37. The laboratory techniques described above used to perform the complementary tasks of hybridization, amplification, and sequencing for the purpose of observing a native gene sequence in a patient sample were well understood, widely used, and fairly uniform insofar as any scientist engaged in obtaining the sequence of a gene in a patient sample would likely have relied on the same techniques and general approach.¹⁸

38. There is nothing about the combination of these routine activities that makes them unique simply because they were used in combination. University of Washington laboratories used such methods collectively as part of genetic testing well before the earliest priority date of any patent raised in Myriad's motion for preliminary injunction relief.

39. For the reasons described above, the use of the well-known techniques to perform genetic testing that relies on the DNA sequence information obtained from a patient's BRCA gene sequences would have been, and was, obvious to those of skill in the art at the time.

40. In fact, University of Washington was performing BRCA1 and BRCA2 testing up until 1998 using amplification and hybridization techniques until the University received a letter from Myriad notifying the University of Myriad's patents in the field of BRCA1 and BRCA2 testing.

¹⁸ See, e.g., Griffin HG, Griffin AM, DNA Sequencing: Recent innovations and future trends. Appl. Biochem. Biotechnol. 38(1-2):147-59 (1993)(“A major innovation has been the application of polymerase chain reaction (PCR) technology to DNA sequence determination, which has led to the development of linear amplification sequencing (cycle sequencing). This very powerful yet technically simple method of sequencing has many advantages over conventional techniques, and may be used in manual or automated methods.”)

41. I was part of a core group of people at Washington University to evaluate whether the University should or would stop performing the BRCA testing in view of Myriad's correspondence.

42. In response to Myriad's correspondence, we decided to discontinue our BRCA testing in the face of a well-funded and motivated corporation hinting that costly patent litigation would ensue if we continued offering the medical tests. As a public research and medical institution, we decided to discontinue our performance of our test because we believed that the risk associated with being engaged in a protracted legal battle against a well-funded, aggressive corporate plaintiff presented an unwanted and unwarranted risk to the overall objectives of our institution and the financial health of our department. The risk of financial harm due to a potential litigation was simply too great to engage in such activities. The decision to avoid litigation by simply discontinuing our performance of the BRCA test for patients was not based on a determination that Myriad's patent claims were patentable or valid.

43. **The Practical Effect of Myriad's Asserted Patent Claims** The asserted patent claims in the preliminary injunction describe routine biological procedures and correlations in mostly generic terms. The act of copying and sequencing the genetic material for purposes of determining its natural composition and the information it encodes is central to the unpatentable biological material's fundamental, natural purpose.

44. For example, For example, Myriad's U.S. Patent No. 5,747,282 filed on August 12, 1994 describes as follows:

'Amplification of Polynucleotides' utilizes methods such as the polymerase chain reaction (PCR), ligation amplification (or ligase chain reaction, LCR) and amplification methods based on the use of Q-beta replicase. These methods are well known and widely practiced in the art. See, e.g., U.S. Pat. Nos. 4,683,195

and 4,683,202 and Innis et al., 1990 (for PCR); and Wu et al., 1989a (for LCR). Reagents and hardware for conducting PCR are commercially available. Primers useful to amplify sequences from the BRCA1 region are preferably complementary to, and hybridize specifically to sequences in the BRCA1 region or in regions that flank a target region therein. BRCA1 sequences generated by amplification may be sequenced directly. Alternatively, but less desirably, the amplified sequence(s) may be cloned prior to sequence analysis. A method for the direct cloning and sequence analysis of enzymatically amplified genomic segments has been described by Scharf, 1986.

‘282 patent, 17:15-32. *See also* ‘282 patent, 16:36-48 (discussing primer design known in the art, and 20:41-53 (describing “techniques for nucleic acid manipulation” known in the art).

45. As a result, the claims at issue in the Preliminary Injunction Motion do not cover novel diagnostic tools or novel methods used in genetic testing. Nor are they analogous to patents on novel medical instruments. Nor do they claim new and inventive methods to amplify or sequence portions of a gene, as the patent specifications acknowledge. Rather, these claims attempt to confer upon their owner the exclusive right to read human BRCA1 and BRCA2 sequences, which the Supreme Court ruled are not patent eligible. The claims either attempt to assert broad ownership over all human DNA sequences that can be used to amplify and sequence BRCA1 and BRCA2, or merely append routine steps to the patent claims, which would necessarily be conducted while assessing the biological relationships between mutations in the BRCA1 or BRCA2 genes and the predisposition to cancer.

46. Myriad’s claim strategy appears to be an overt attempt to claim and exclude access to natural products and laws of nature by simply using the more abstract patent concept of a ‘method’ or ‘process’ directed to same.

47. Attached hereto as Appendix 1 is an analysis of the asserted claims that shows how Myriad has extended the breadth of its composition claims simply by appending the concept of the BRCA1 and BRCA2 genes to merely include routine procedures that were well-known in the art so as to preempt access to the gene and its embedded, medically-relevant information.

See Tait Appendix 1.

48. Myriad's asserted patent claims attempt to impede access to the genes' nucleic acid sequence information by claiming the only available (and obvious) laboratory means needed to determine it. As a result, Myriad effectively seeks to enforce a *de facto* patent on the unpatentable genes, which is injurious to the public at large.

49. Previous courts recognized that the tools and methods used in the initial isolation of the BRCA1 and BRCA2 genes were in routine use at the time the biological facts of the associations of mutations in these genes to hereditary breast and ovarian cancer were discovered. Moreover, the key steps in genetic testing, DNA extraction, amplification, and sequencing can now be performed using routine, automated methods. Nevertheless, Myriad Genetics claims the exclusive right to read and compare gene sequences using irrespective of method, whether in existence now or in the future.

50. Due to Myriad's monopoly, physicians and clinical laboratory technologists in training cannot receive clinical instruction in the performance and interpretation of data from the BRCA tests. The public is thus deprived of trained health care providers with special expertise in this area.

51. Due to Myriad's monopoly, other clinical laboratories are unable to conduct BRCA1 or BRCA2 tests, the results of which are a key resource for research information. For example, clinical testing by DNA sequencing can often reveal variants of uncertain significance (VUS): specific DNA sequences in a patient that are different from the common reference sequence, but whose clinical significance is uncertain. Only through further research, data sharing, and publication can the clinical significance of these variants be determined. When there is a monopoly on BRCA testing, the public is forced to accept Myriad's sole interpretation of variants of uncertain significance based on Myriad's secret and proprietary database of DNA sequence results for patients with these variants.

52. A long-standing monopoly on testing has resulted in Myriad's becoming complacent with its outdated and now inferior testing technology. Next-generation sequencing provides more comprehensive testing than Sanger sequencing, and can detect certain disease-causing mutations that cannot be detected by standard Sanger sequencing. For example, due to its high sensitivity and ability to report the sequence of individual DNA molecules, next-generation sequencing can detect the presence of genetic mosaics, i.e., people who have two populations of cells, a minor population with a deleterious mutation, and a major population without a deleterious mutation. Because Sanger sequencing reports the average sequence of the entire population of cells, it will often miss the presence of genetic mosaics. A person who is a genetic mosaic with a minor population of mutation-positive cells undetected by Sanger sequencing can still be at high risk of cancer, because mutation-positive cells can enter the pathway of carcinogenesis and eventually give rise to cancers of the breast and/or ovary.

I declare, pursuant to 28 U.S.C. § 1746, under penalty of perjury under the laws of the United States, that the foregoing is true and correct to the best of my knowledge and belief.

Jonathan Tait

Jonathan F. Tait M.D., Ph.D.
August 14, 2013

CERTIFICATE OF SERVICE

On August 14, 2013, I served a copy of the foregoing, by electronic case filing (ECF), by e-filing the above-referenced document(s) utilizing the United States District Court, District of Utah's mandated Electronic Case Filing service, which service automatically e-served a copy of the document(s) upon confirmation of e-filing to all counsel in this case registered to receive e-filing notice, and additionally by electronic transmission by attaching the referenced documents or link to the referenced documents to an electronic mail and transmitting the same to the e-mail addresses indicated below as follows:

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/s/ *William G. Gaede, III*

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